PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference DI-13-C6-PCT	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/US04/09135	International filing date *(day/month/year)* 25 March 2004 (25.03.2004)	Priority date *(day/month/year)* 27 March 2003 (27.03.2003)
International Patent Classification (IPC) or national classification and IPC IPC(7): G01N 33/53 and US Cl.: 435/7		
Applicant HESKA CORPORATION		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *(sent to the applicant and to the International Bureau)* a total of ___ sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☐ Box No. II Priority
   - ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☒ Box No. VIII Certain observations on the international application

Date of submission of the demand 20 October 2004 (20.04.2004)	Date of completion of this report 29 April 2005 (29.04.2005)
Name and mailing address of the IPEA/ US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Deborah A. Davis for Laurence Telephone No. (572) 272-0818

Form PCT/IPEA/409 (cover sheet)(January 2004)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US04/09135

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ the international application as originally filed/furnished

☒ the description:
pages 1-48 as originally filed/furnished
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____

☒ the claims:
pages 49-51 as originally filed/furnished
pages* NONE as amended (together with any statement) under Article 19
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____

☐ the drawings:
pages NONE as originally filed/furnished
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☒ The amendments have resulted in the cancellation of:

☒ the description, pages NONE
☒ the claims, Nos. NONE
☒ the drawings, sheets/figs NONE
☒ the sequence listing (*specify*): NONE
☒ any table(s) related to the sequence listing (*specify*): NONE

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing (*specify*): _____
☐ any table(s) related to the sequence listing (*specify*): _____

** If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 5, 6 and 8

because:

☐ the said international application, or the said claim Nos. ____ relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 5,6 and 8 are so unclear that no meaningful opinion could be formed *(specify)*:

No meaningful search could be could be established for the above claims because the names of these antibodies are not art recognized. (PCT Rule 6.4(a).

☐ the claims, or said claims Nos. ____ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. ____

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
☐ has not been furnished
☐ does not comply with the standard

the computer readable form
☐ has not been furnished
☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims NONE	YES
	Claims 1-17	NO
Inventive Step (IS)	Claims NONE	YES
	Claims 1-17	NO
Industrial Applicability (IA)	Claims 1-17	YES
	Claims NONE	NO

2. Citations and Explanations (Rule 70.7)
Please See Continuation Sheet

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US04/09135

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1-2 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claims 1-2 are indefinite for the following reason(s): Claims 1-2 recite the same ranges of albumin and specific gravity for the detection of early and late renal disease, therefore it is unclear as to how early renal disease can be distinguished from late renal disease.

Claims 5-6 and 8 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claims 5-6 and 8 are indefinite for the following reason(s): The claimed subject matter do not contain art recognized terms and therefore no meaningful search could be established.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

V. 2. Citations and Explanations:

Claims 1-3, 7, 9-11, 15-17 lack an inventive step under PCT Article 33(3) as being obvious over Suzuki et al (USP#4,246,835) in view of Lau (USP#5,087,575), in view of Zimmerle (USP#5,043,744) further in view of Zimmerle (USP#5,403,744) and in further view of Zhang et al (USP#6,214,813).

Suzuki et al teaches a method of diagnosing renal disease by detecting fragments of albumin in human urine. The detection is carried out by immunological methods (see abstract), such as EIA and immunoblot techniques (column 2, lines 63-68). All protein contained in a urinary sample to be assayed are solubilized by treating the sample in boiled water for a certain period to inactivate the proteases contained in the sample (column 4, lines 45-55). Separated human albumin and the human albumin fragments are transferred to a support and visualized by utilizing an immunoblot method (column 3, lines 35-40). Detection was carried out at room temperature (column 13, lines 17-35). Suzuki et al also teaches accurate quantitative determination of urinary albumin may be carried out by RIA and immunoprecipitation with commercially available kits that contains anti-albumin antibodies and albumin-immunized latex, wherein latex is agglutinated by the antigen-antibody reaction (column 1, lines 29-46).

Suzuki et al is silent with respect to teaching the particular ranges of albumin levels is diagnostic of renal disease.

However, the reference of Lau teaches that the concentrations of protein in urine should be minimal to non-existent because abnormally high amount of albumin and/or low-molecular weight proteins in urine must be detected and related to a renal disease (column 1, lines 49 - column 2, lines 1-15). Lau discloses a method of assaying urine for proteins at low to trace quantities ranging from 0 mg/dL to 2000mg/dL (columns 6 and 7) which encompasses albumin ranges in the instant invention. Lau utilizes test strips (dipstick-base assay) that are dipped into urine samples that has a dye indicator and for each albumin concentration; the specific gravity of a urine sample was adjusted from 1.007 to 1.032 (column 22, lines 47-67).

Lau does not teach the specific gravity of urine is indicative of renal disease.

However, the reference of Zimmerle teaches that abnormally high or low specific gravities are clinically significant. But, urine with a fixed low specific gravity of approximately 1.010 that varies little from specimen to specimen is known as isothenuric which is a condition indicative of severe renal damage with disturbance of both the concentrating and diluting abilities of the kidney.

Zimmerle does not teach obtaining a urine sample from a felid or equid to determine the amount of albumin.

However, Zhang et al. teaches a method of lowering protein levels in urine, by administering to a patient an effective amount of a compound or pharmaceutical composition orally, intravenously or around the kidney (page 9, paragraph 0121). These pharmaceuticals are therapeutic. The patient of interest could be felines, equines, canines (page 7, paragraph 0096) used in animal models for

Supplemental Box

experimental investigations of human disease.

It would have been obvious to one of ordinary skill in the art to modify the reference to Suzuki et al to include the correlation of particular albumin concentration ranges as taught by Lau because differentiating between low protein concentration levels is clinically important in the art because a range of from about 10mg/dL to about 20mg/dL is used as the normal urine protein level for a healthy individual, therefore urine protein levels from 0 mg/dL to 10mg/dL may indicate an excessive excretion of proteins that can signify a diseased state. It would have been further obvious to one of ordinary skill in the art to modify the reference of Suzuki et al to include the teaching of specific gravity at the range of 1.010 as taught by Zimmerle, to identify patients with severe renal damage. It would have been further obvious to one of ordinary skill in the art to determine albumin levels in the urine of felids and equids because they are used as animal models for experimental investigations to explore human disease.

Claims 12-14 an inventive step under PCT Article 33(3) as being obvious over Suzuki et al, in view of Lau, in view of Zimmerle, in view of Zhang et al, and further in view of Morrison et al (USP#804,625).

The teachings of Suzuke et al, in view of Lau, in view of Zimmerle, in view of Zhang et al are set forth above but does not specifically mentions the use of enzyme-linked assays and a single-step.

However Morrision et al teaches assay procedures for ELISA's and homogeneous (single step) assays. Morrison discloses that as many as 2,000 assays by a technician employing a solid-phase ELISA in microtiter plates and these thpes of assays can be performed in a homogeneous assay (single step) format which bound and free labeled material need not be separated (column 2,k lines 9-32).

Therefore, it would have been obvious to one of ordinary skill in the art to modify the teachings of Suzuki et al, in view of Lau, in view of Zimmerle, in view of Zhang et al above to include homogeneous (single step) and ELISAs assay formats as taught by Morrison et al because detection of analytes can be performed without laborious separation steps (column 2, lines 9-32).

Claim 4 lack an inventive step under PCT Article 33(3) as being obvious over Suzuki et al (USP#4,246,835) in view of Lau (USP#5,087,575), in view of Zimmerle (USP#5,043,744) in view of Zimmerle (USP#5,403,744) in view of Zhang et al (USP#6,214,813) and further in view of Zuk et al (USP#4,281,061).

Zuk et al teach as a matter of convenience the reagents can be provided as kits, where the reagents are in predetermined ratios, so as to substantially optimize the sensitivity of the assay in the range of interest (column 2, lines 63-66). Further, the reagents in a kit are available in pre measured amounts which eliminates the variability that can occur when performing the assay.

Claims 1-4, 7, 9-17 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.